Dowling, John 2004

Dr. John Dowling Oral History 2004 A

John Dowling Interview

Interviewer: Edward McManus

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Mr. McManus: I think we first did program planning at the Harvard Club in 1973. It could have been later when we did it there because Alan Laties was part of that group. But do you remember? Not that you necessarily have to, but I was kind of remembering things.

Dr. Dowling: I was involved in more than one of the program plans.

Mr. McManus: Do you remember when you first were?

Dr. Dowling: Now you're asking a very hard question. I am not sure.

Mr. McManus: I think it was early on, either the first or the second,

Dr. Dowling: I did consult on many of them, pretty much up to the last two or three where I haven't been so involved.

Mr. McManus: What is your view? Because we have to write a chapter on Program Planning. I'm going to start the chapter off with a quote from Tom Kennedy who was then Associate Director of NIH for Planning, and later on was the Vice President of the AAMC. When we asked Tom about planning back when the Eye Institute started, he said we didn't do planning at NIH. It depended upon the individual genius of the scientists to give us directions where we were to go and I think generally that was the attitude of the scientific community.

Dr. Dowling: I think program planning has been extraordinary valuable as I understand it and remember it. And I think the Eye Institute was the first of the Institutes to do program planning.

Mr. McManus: I think Cancer did it long before.

Dr. Dowling: Maybe so, but anyway, I think it's useful every four or five years to see where a field is, where it might go and where resources might be most profitably put. And that was always the idea behind the program planning. Although it's nice to leave program planning to individuals, what tends to happen in science, in my view, is that people swarm. There's a topic that is hot and everybody is focusing just on that, and they're beating it to death. But on the other hand, there may be something that really is ripe for the taking, and yet no one is working on it. And this is where program planning is very useful in my view. To point out opportunities that people have not appreciated. I think it also is important to designate areas of high program relevance. That is, where you really need a few grants researching a particular problem, and program planning is very useful for that as well. From my perspective whenever a new plan came out, I would read it carefully. I found over the years that they were done thoughtfully and were of great use in thinking about where the next areas are in which we can really make advances.

Mr. McManus: One of the interesting things that I had sort of forgotten because it's interesting when you look at the history of the planning, Carl was responsible for making sure that the science guys did the right things—he knew where the dynamics were. There was a management framework that kind of tied in with management by objectives and in the government performance by objective kinds of things that come later that I had sort of done and that was kind of my background and I kind of kept it quiet but that was why we were somewhat sort of semi legitimate with the management folks. But one of the things that happened, and probably was for the good, and I don't want to make a big deal about it—priorities were very important but it was always very difficult because of the scientific priorities, in terms of there's the priorities for grants, there's always priorities and it always cost lots of problems. And I thought that the fourth plan and I'm not forgetting this—priorities were changed to mean what are the most important research questions. It was really very good—it was the right way to do it.

Dr. Dowling: I always thought we did this from the beginning and did it right

Mr. McManus: We did, and we called them priorities and then they stopped calling them priorities.

Dr. Dowling: The program planning documents were very important for young investigators, who had just finished their training and starting their first position. They would get a document like this and could see what the guru's in the field say about where the next profitable areas are. For many of the young people, they would say, "that's an interesting question and an interesting problem and I think I can contribute to that." The program planning effort was extraordinarily useful right from the beginning and I hope it continues.

Mr. McManus: I think it will.

Dr. Dowling: All institutes should be doing it.

Mr. McManus: One of the purposes of this book is hopefully will be to get Paul to read it and kind of see some of the background of all of this.

Dr. Dowling: Which will be good. I do think Paul appreciates it.

Mr. McManus: No, he does. We have forgotten all lot of why we did things and I want to put all of those back on the record. Even back before the planning there was the beginning of the Institute. Where were you when the Institute began in 1969 and 1970?

Dr. Dowling: I was still at Johns Hopkins. I had finished my graduate degree at Harvard in 1961, stayed on at Harvard until 1964, first an instructor and then an Assistant Professor and then in 1964, I moved to the Wilmer Institute. So my first grants came from NINDB.

Mr. McManus: Mildred Weisenfeld. And I also now understand why Mildred Weisenfeld was so important.

Dr. Dowling: The Eye Institute began in 1969; my grants went to the NEI in 1970.

Mr. McManus: Do you remember any of the feelings or interactions from the Scientific side of community rather than the eh, about a new institute, whether this was a good thing or whether it was…

Dr. Dowling: I think we all thought it was a good thing - that it would put the eye in the forefront in a way that it tended not to be in the neurobiological and neurological communities. This is still the case. It is astonishing how many people I still meet who think the retina is part of the peripheral nervous system. That's why when I wrote my book in 1987, I called it "The Retina: An Approachable Part of the Brain" to make the point that the retina is a part of the central nervous system and the mechanisms that one can mine from study of the retina, whether it be disease mechanisms or just normal structural, functional and developmental mechanisms, have applicability to the central nervous system. And when you look back on some of the findings that have been made first in the retina and that subsequently were made in the central nervous system, it's amazing how much the retina has really contributed.

Mr. McManus: Like what?

Dr. Dowling: The regulation of gap junctions by second-messenger systems is one. Also, the regulation of glutamate channels by second-messenger cascades is another that was first shown in the retina. CNS people believe the latter finding was first made elsewhere in the CNS, but not so. The retinal work was four or five years earlier. I mean things of this sort.

Very early on one could also begin to work out the neurocircuitry in the retina in a way that still isn't impossible in much of the rest of the CNS. Another huge breakthrough relates to Retinitis Pigmentosa (RP) which in my view is the best understood neurodegenerative disease of all. And the underlying genetics that has been worked out in Retinitis Pigmentosa goes way beyond anything that has been shown in other neurodegenerative diseases. We still talk about Alzheimer's as one disease. But, like RP, it's going to turn out to be a hundred diseases.

Mr. McManus: Just as I have said the classification of the disease is very important. Because of the clinical trials of Berson's, we now can classify R.P. Whether or not you like the results of those trials they had to be very, very scientific to classify the patients who have RP.

Dr. Dowling: Another example is the visual transduction process in vertebrates, where cyclic nucleotide channels were first found. The genetics of the cone visual pigments, worked out by Jeremy Nathans, is one of the great triumphs of modern neuroscience as is the elucidation of all the visual transduction mechanisms. A number of people have contributed to this and the work is still going on, but it is a tremendous advance.

Mr. McManus: Help me with a thought. See, we're going to do one of the chapters, probably the last chapter will be the impact of the NEI and I think that we are going to do lots of things and Carl is going to do that—but I think one of them would be— and he has said lot of the same things that you just said, but I think one of them would be the opening up a neurobiology with the kind of things you said so we can put it in one place and have it as a reference. There are a lot of stories of discovery that NEI that has done. I don't know if you have seen them, they use them for the Congressional Budget Justification. We started that under Varmus. I was on the committee and we were looking for ways to jazz up the Congressional Justifications and we came up with this idea, well let's do a whole story of discovery on vision research and I think a lot of what you just said may be in there about the retina. It was the first story that we did. So I think we have a lot of this but so Carl may be talking to you separately.

Dr. Dowling: That will be fine. I'll be glad to do it.

Mr. McManus: I think that would be a nice thing to do. That's one of the problems, people forget the story and never knew the story and so we want to do this.

Dr. Dowling: What the Eye Institute did was to put focus on study of the eye. It brought many people into the field without question. Part of the reason many people came into the field was that they began to see the successes that people studying the eye were having. Think back to the beginnings of ARVO when it started in its modern form in 1968, there were only about 150-170 people there.

Mr. McManus: Yeah, the first few years I was there it was only about 200 people there.

Dr. Dowling: Last year 8,000 attended the ARVO meeting. It is just unbelievable how much the field has grown and how sophisticated it has become. So the Eye Institute has had a huge impact. I think its emphasis on individual research grants is also something that needs to be emphasized. This gave real priority to the individual investigator. And other of the Institutes, including the old NINDB with its huge program project grants, did not emphasize the individual investigator as much as the Eye Institute did right from day one. I think this was a good thing then.

Mr. McManus: How are about now?

Dr. Dowling: Now, I think we need to start thinking more in terms of interdisciplinary programs and mechanisms for fostering that. I guess what I worry now about the eye community is that although it's had great successes, it has grown a little parochial. It will be useful to find ways to encourage more cooperative ventures.

Mr. McManus: To do both.

Dr. Dowling: To do both, that's right.

Mr. McManus: I want to make sure, you see I have that—because Carl is still back on the R01s and I sort of, when I left started getting into more corporate endeavors, like we have cooperative clinical trials?

Dr. Dowling: Yes that's been useful.

Mr. McManus: Let's do cooperative kind of research proposals. Like we started of with some of the genomes research and stuff I mean, if you going to do anything with manipulating the genome you need all kinds of different people and you need some mechanism to bring them all together. So they started with some of those…

Dr. Dowling: Right, life does change. In the early days the emphasis on the individual investigator by the Eye Institute was just the way to go and I think it really maximized the bang for the buck.

Mr. McManus: I like when you said that the emphasis on the individual investigator, I never heard it put that way and that's good, and that's what we did, you're right. Let me ask you about—there were a few people that did not want to—let's see who was it that Carl was talking to somebody who said that he was not too interested in going to the Eye Institute. Actually, Carl when he was first approached he had two grants with neurology and Everett Kinsey approached him. Carl said, "What am I going to fool around with success for, I am doing great over here." Everett gave him all the good reasons why he should do it.

Dr. Dowling: Much of the credit for the explosion of research in all aspects of eye and vision research has to be given to the Eye Institute. Its support of the ARVO meeting was also critical where the emphasis from the beginning was making sure that it was not just psychologists talking to psychologists, electrophysiologists to electrophysiologists, and anatomists to anatomists, but bringing everybody together - the clinicians and basic scientists, and researchers from medical schools, research institutes, colleges and universities

Mr. McManus: I was thinking of asking you this question and I did not know how to put it, the relationship because it was somewhat controversial at certain times but Carl certainly felt that our goals were very, very important sometimes too important—right Carl? (Laugh, because he will see this) but it was very important I think that there be a strong professional organization and I think that Carl and I met you, Nigel Daw, and Art Silverstein back when we where talking about moving the ARVO office to Washington.

Dr. Dowling: Yes, from a basement in New York.

Mr. McManus: From the basement in New York, the things like that.

Dr. Dowling: To make it more of a national organization.

Mr. McManus: And certainly Carl actively pushed that.

Dr. Dowling: He was very supportive of it over the years. The first time I went to ARVO was back in 1961. It was a small ophthalmic research meeting. There were only about 150 of us there. My brother was a resident at the Eye and Ear and he gave a paper and I gave a paper. I had just finished my graduate work with George Wald, and the meeting was dominated, of course, by clinical papers. In fact, my paper was on Vitamin A deficiency and night blindness. It was 1967 or so that Ed Maumenee gathered a group of us at The Wilmer Institute - Art Silverstein, Morris Langhan and myself and told us that the ARO Board Trustees felt that they really wanted to broaden the meeting and how might we do this? From that meeting we made the suggestion that if we fashioned ARO after the old FASEB meetings - the Federation of the American Societies of Experimental Biology or something like that - we could have sections that represented all aspects of vision research. Ed brought that to the Board and they were enthusiastic. A number of us became involved, including myself who was asked to form a section in electrophysiology, and Art Silverstein one in Immunology. We then approached Neil Smeltzer at Columbia to do one in anatomy and Richard Blackwell at Ohio State to do one in psychophysics and that's when we really got ARVO up and running in its modern form. That first year we wrote to people asking if they would be willing to come to a meeting with the main focus of the meeting being on sections that emphasized electrophysiology, anatomy, or what have you. And the meeting really took off at that point, and became, within a short time, a national meeting. Let me tell you a story that involved the governance of ARVO and how it was broadened.

It was when we were in Sarasota, and there were probably four or five hundred people at the meeting. The trustees were then all ophthalmologists, and there was some talk among a number of us in basic science that if ARVO was to represent all of vision research, the Board of Trustees should include not only ophthalmologists, but basic vision researchers as well. But how to accomplish this? I approached Ed Maumenee and a couple of other people, but they felt that the organization should be run by the ophthalmologists. But what then happened, and how it happened is an interesting story. Marvin Sears was one of the nominees that year (I can't remember which year it was although I could figure it out by looking at the list of when people were elected Trustees). He was annoyed about something that ARVO did and the morning of the election, he pulled out so there was only one person nominated, an ophthalmologist. Our bylaws said there had to be two people running. I heard about the situation at lunch time, and soon there was group of us who asked who might we ask to run? I suggested Lorrin Riggs and everyone thought he was the perfect choice. I tracked Lorrin down and found him in the water in front of the Sand Castle Motel. I joined him in the water and said, "Lorrin, here is the situation. Would you be willing to run if we nominate you at the business meeting this afternoon?" He said, "John, I would be willing to do that." He was a very distinguished scientist - a member of the National Academy of Sciences…

Mr. McManus: And a nice even personality.

Dr. Dowling: Yes, a very even personality. So I came out of the water and began talking to people who then talked to other people. When the business meeting began, most of the people at the meeting were basic visual scientists. I nominated Lorrin and he won by a landslide. Ed Maumenee was furious with me, but he soon got over it and eventually appreciated the change.

Mr. McManus: Was Maumanee the leader of the organization?

Dr. Dowling: I don't remember, but I think he was still on the Board of Trustees.

Mr. McManus: And I think that Lorrin became President.

Dr. Dowling: Lorrin did eventually become President. He was highly respected and not at all confrontational. He was the perfect choice to be the first non-ophthalmologist on the Board.

Mr. McManus: He was.

Dr. Dowling: And I think the organization has done extraordinarily well since then.

Mr. McManus: I'll ask you a question that doesn't directly relate to this but then again it does, in kind of writing this thing up and why there was a separate Eye Institute. You talk to different people and look at some of the history and look at some of the testimonies especially and people say… Oh I know, we were talking to the former Associate Director for Extramural of NIA and to the former Director of the Neurology Institute, Maury Goldstein. He was talking about well, the ophthalmologists were not happy because their grants weren't getting funded and I'm thinking you know…

Dr. Dowling: That's not it at all.

Mr. McManus: Look at the guys that you mentioned Wald, and you know Wiesel were in the pipeline, you were in the pipeline, there were others that had received grants such as Hartline.

Dr. Dowling: Hartline, of course.

Mr. McManus: There were lots of vision guys probably more than in Neurology.

Dr. Dowling: That was not the reason at all in my view; rather, it was that that more emphasis on eye and vision research was needed. As I noted earlier, I would go to brain meetings, and people would listen to what I had to say. But what I was talking about with regard to retinal mechanisms did not seem to them to have any relationship to *brain* mechanisms. The retina, in their view, was apart of the peripheral nervous system.

Mr. McManus: We had a distinguished group of people already in the department, more distinguished than a lot of fields. That's something that I thought was uh… Do you remember your first formal involvement with the NEI was? I would even consider it if it was just serving on study section.

Dr. Dowling: I was asked to be on study section fairly early on, certainly when I was in Baltimore. That would have been in the late 1960's. Marie Jakus was our Study Section secretary.

Mr. McManus: Then you were involved in program planning.

Dr. Dowling: Yes, I was involved in various Program Plans.

Mr. McManus: When did you go on council? Maybe in the '80s?

Dr. Dowling: Yes, I was on Council - with Ben Berman among others - and it probably was in the 80's. I was on Study Sections for several years, and also involved in several Program Plans. One year I was in charge of the retinal part of the Program Plan and had primary responsibility for it.

Mr. McManus: One of the things that I am doing in the Planning chapter when I talk about how difficult it was to do planning taken from the quote I gave you from Kennedy and there were a lot of people that were for it, but there were a lot of basic scientist that questioned it. Did you ever run into any problems with any of them who said to you we can't plan for this?

Dr. Dowling: No, I don't think so. At least the people I worked with over the years that were on committees I was on or that I chaired, all had real interest and enthusiasm for the project. They showed an understanding that this was a very valuable thing to do.

Mr. McManus: Better get their interest because I think it was a big communication vehicle.

Dr. Dowling: Certainly as the plans came out I would get comments from people who had read them, indicating they were useful. Comments such as "One of the things that the committee pointed out seems very interesting to me and I am going to put in a grant to do that." And that's exactly what we wanted to have happen.

Mr. McManus: We had Morton Grant who wrote the first glaucoma report and then he put in a center grant for everything that was in there. (Laughter)

Dr. Dowling: That's good management.

Mr. McManus: It was. Let me ask you, when you were on the council because as I'm doing the program planning and some of the other things I think the interaction with the Council and the institute management was so important and what were your views of the Council role when you were on it?

Dr. Dowling: We certainly were asked our opinions of many things by Carl. I never felt, though, that we had very much clout with regard to changing NEI policies. While I was on Council, most of the focus was on the funding of grants and program planning. We also discussed the fairness of study sections and what we should do about high program relevance, and so on so forth. So from that point of view it was very valuable. Maria Giovanni was just coming on to Eye Institute staff, and she and I had a wonderful working relationship. That is, she would send me all of the rebuttals submitted to Council, and we would talk about them before hand. If I felt a proposal should go back to Study Section because the review did not seem appropriate, or that we should suggest another option, I would discuss it with her, so by the time things came to Council, we had our ducks in order, so I thought it was quite a good process. We were not providing a second level of review or second guessing the Study Sections, but if we saw something that did not seem quite right, we would send the proposal back or suggest another Study Section. That's what I remember was the main role of the Council when I was on it.

Mr. McManus: And certainly, when I was going back to look at the first charter for Council, the only thing in there was to review grants and there was no mandate to do program planning or anything like that except priorities, do the long range budgeting and then of course we put that in, and that was really for us, I guess it was a big cultural change. The idea of making council sort of a Board of Directors and bringing all… that wasn't in it probably was a good idea however we thought that we were already breaking the mold on it…and it has been lots of discussion about that and probably is something that will happen some time in the future.

Dr. Dowling: Carl would certainly often talk about procedures and policies for the Eye Institute and we would give our opinions, but we were never asked to vote on any of these things, but we would give feedback to him. Issues such as the lower priority of program project grants versus individual grants were supported very strongly by the Council.

Mr. McManus: The big thing, the big policy thing looking back at the history of the Eye Institute and benefiting from looking back at the minutes and reading where you were very active was advising us *not* to negotiate grants downward because of overall budgetary problems.

Dr. Dowling: Yes.

Mr. McManus: Remember that? Everybody else was negotiating 10, 20, 30% I mean it was ridiculous and we just didn't do it. We didn't do it. And you were the main one behind it, right?

Dr. Dowling: That was a big issue, but I don't remember being the prime mover on that issue. The issue I remember I did get steamed up about was the pressure to focus much more extensively on mammalian particularly primate vision research, which came, I believe, mainly from Ken Brown.

Mr. McManus: In indirect costs. Yeah, I'm still in trouble with Steve Ryan because of what Ken did to me in indirect costs which I still sort of believe in.

Dr. Dowling: I felt that focusing on primates was short sighted, that we could still learn an enormous amount not only from cold-blooded vertebrates, but also invertebrates. A number of very good people working on invertebrates became discouraged about getting funding from the NEI to do that kind of research and thus they moved into vertebrate research. In at least one case, I won't mention names, I don't think they did nearly as good work as they had done previously.

Mr. McManus: They might have done well.

Dr. Dowling: The other thing I remember is that Carl questioned the number of NEI supported rhodopsin grants. Should we be supporting as many as we were? I recall him saying "I don't see any relationship of rhodopsin research to disease" and of course we know what happened thereafter. The first genetic mutation in retinitis pigmentosa was in the rhodopsin gene and now we now of at least 70.

Mr. McManus: Well, you know one of the advantages was that we had a forum to discuss these issues—the Council meeting.

Dr. Dowling: That's right.

Mr. McManus: Whereas, these decisions might have just been made in one of the other institutes with out any discussion.

Dr. Dowling: No, we did have a chance to voice our opinions and we did. It all worked out very well.

Mr. McManus: And then, then you know, kind of skipping along a lot of it. You have already said some of the advances that you think that came about that were supported by the NEI, do you want to add to any of those? You talked about the gap junctions and …

Dr. Dowling: Certainly the work unraveling the phototransduction process in the photoreceptors was exceptional, with the big breakthrough coming in about the mid 1980's.

Mr. McManus: And that is one of the stories of discovery and we have that very well written up.

Dr. Dowling: That was phenomenal. Understanding retinal mechanisms is another triumph where a number of neural mechanisms were unraveled in the retina first before they were seen elsewhere in the central nervous system. The whole RP story is another fabulous example. And then bringing us to the present day, there is no doubt in my mind that the place where gene therapy is first going to work is going to be the eye, because we have an encapsulated system where we can put a vector sub-retinally into a collapsed ventricle.

Mr. McManus: It's interesting you know. I was way out on that band wagon 10 years ago but it was too early. I don't always appreciate Harold Varmus, but I usually do scientifically. We were having a meeting with him about scientific priorities in vision and we said we were interested in gene therapy. Gene modification and like that and he said, "be careful." And I said, oh, were going to have a conference and this guy Jim Somebody-or-other from the University of Pennsylvania was going to lead it. He left subsequently, he had some problems, he was a big gene therapy guy and he is going to be there and Varmus said, "Well, this is a really complicated. There are all kind of things happening…" he said. He is a basic scientist and he knows that the world is…, and we backed off. And he was right. It was ten years ago and it was a lot more complicated than maybe some of us thought.

Dr. Dowling: It required development but it's come along very well. Hubel & Wiesel's major work occurred before the Eye Institute was established, their great discoveries were made the early the 60's. But certainly that work emphasizes how vision can play such a leading role in understanding the brain mechanisms. The story of visual deprivation is telling us so much about brain development and that is something the Eye Institute should take credit for.

Mr. McManus: We will.

Dr. Dowling: Much of their later work was supported by the Eye Institute - I mean Dave and Torsten's grants - by the late 1960's or early '70's.

Mr. McManus: In ’69. In fact I could not meet up with Dave, I hope to still see him. Not today, but I’ll see him later. But he told Carl, and I want to verify this that he wanted to have his grant transferred over to a new Eye Institute and we solicited him, which is nice because he was already a big name and going in the right direction and that was really important to Carl. We did the scientific advancement, now how about the famous Dowling Report on the Intramural Program, which we referred to as the Dowling Report.

Dr. Dowling: Yes, I did chair that committee as you well know. In the early days of the National Institutes of Health the Intramural Program was sterling, and then for a variety of reasons, it slipped.

Mr. McManus: People were there forever.

Dr. Dowling: Yes people were there for too long and it didn’t have that cache or brilliance that it did in the early days. This was the case not only for the Eye Institute, but for a number of Institutes as well.

Mr. McManus: Yes, yes.

Dr. Dowling: When we came and looked at the Intramural Program I felt it needed an enormous amount of rejuvenation. There certainly were some excellent people there like Joram Piatagorsky and Graham Wistow who are very good (and it’s too bad that they don’t get along a little better) so there were excellent people there, but it seemed clear that one needed to rethink the Intramural Program in many ways. First, investigators should not be there forever. Second, it should be a place where very high risk research is done, but exactly how to get it to work that way is a problem.

Mr. McManus: Yeah, I had all kinds of ideas at one time about 10 year appointments and stuff like that.

Dr. Dowling: I think that’s not a bad way to go at all. I mean there were some great successes there including, of course, Bob Wurtz and his group. He is one of the top people today in vision research.

Mr. McManus: But also you know, there are certain areas of research that are long term anyhow. So in Bob Wurtz’s case, once you pick a really bright guy at the front you know that he’s going to spend his life and two or three other lifetimes figuring out how the brain works. In these other areas where you’re in for 5 or 10 years, recognize it.

Dr. Dowling: I think that’s right. It’s tough, though, to get very good people to come to the NIH under these circumstances; that’s the problem.

Mr. McManus: Have two appointments.

Dr. Dowling: Excuse me?

Mr. McManus: Have two appointments.

Dr. Dowling: Right.

Mr. McManus: I mean there are always ways to do it if you really…

Dr. Dowling: I think we pointed that out. We did not pull many punches.

Mr. McManus: No, you didn’t.

Dr. Dowling: But I also think it wasn't just the Eye Institute. Other Institute Intramural Programs had slipped.

Mr. McManus: No, in fact I was reading, there was a sort of a history in the Neurology Institute done on something for their 50th Anniversary and they had a section about the interview and it was very interesting how we got…the fellow who wrote it was a professor from Columbia. Rallings, I think his name was, you may know him. But he said that Varmus had commissioned studies of the Intramural and they were one of the first ones and there were lots of problems in NINDS, and because of the things that we talked about. Then there was a complete overhaul of the NINDS intramural program.

Dr. Dowling: When I think of the most successful era for the Intramural Program at the NIH and perhaps the most successful of the Intramural Programs, it was probably that of Seymour Kety of the National Institute of Mental Health. He had cornered an astonishing group of researchers.

Mr. McManus: There was no Biology in Mental Health research. He started it with Axelrod and many others.

Dr. Dowling: Right, but eventually most of the people moved on.

Mr. McManus: Evarts was an exception.

Dr. Dowling: Even Hubel was there at one point..

Mr. McManus: Oh, was Hubel there?

Dr. Dowling: Hubel was there.

Mr. McManus: See I took uh.

Dr. Dowling: Part of it was that it was the time of Viet Nam.

Mr. McManus: When you could get the two year…

Dr. Dowling: This was the two year appointment substituting for military service, so you get the best and the brightest, and we don't have that now.

Mr. McManus: You will.

Dr. Dowling: I don't think that will happen.

Mr. McManus: Just on the side, when I was going to come earlier, you reminded me that you couldn't do it then because you had to vote. I'd forgotten about the election, but I stayed home and voted but it didn't do any good, but…(laughter).

Dr. Dowling: Was I depressed, but life goes on. Where were we?

Mr. McManus: We were talking about the Intramural Program.

Dr. Dowling: How to set up the Intramural Program to keep it vital, young, continually turning over and focusing on high-risk research; that's what makes it tough.

Mr. McManus: You know, that may be the easiest question. There are other bigger questions about the NIH as a whole that need to be addressed like how they're going to interact with these state programs like California. Nobody's going to turn away 3 million a year or whatever it is, and other states are going to do the same thing to try and compete. What is that going to do to the NIH? There used to be there was an old proposal several years ago to regionalize all of NIH, you know give the formulas (?) back to the states. Well if you have a big state, NIH is anyhow, so there are all kinds of things that need to be looked at and thought about for the future.

Dr. Dowling: I looked at the California initiative as an attempt to get biotech industry in that area.

Mr. McManus: Yeah, right.

Dr. Dowling: You said something else earlier that I might comment on that doesn't have to do with what we're talking about. It is that we are moving more and more toward translational research which I think is really important. We are trying to bring discoveries to market. However, clinical trials cost an enormous amount, I'm not suggesting at all that we cut back on those clinical trials - it's essential that we find out whether a drug is safe, or whether it is efficacious and so on and so forth. But I think it means that we will need to build more partnerships between government and private industry. And whereas we have some, such as the small business grant awards, they are really too small.

Mr. McManus: There are lots of partnerships in the drug area, but there are lots of problems. And I remember that I tried to promote a lot of partnerships. Pharmaceutical companies rightly do not want the government to be involved in their studies as they want to keep the information private and it may be that only the government should do the studies and maybe they should be paid for by the pharmaceutical companies and only the government can do it—I don't mean the government, I mean only the universities. So that's something that could be looked at. It's a partnership it will have to be a partnership but maybe somebody else…

Dr. Dowling: A big problem is that drug companies don't want people to know the results of some of their trials.

Mr. McManus: I mean just look at this Merck, Vioxx thing. If that had been done like we did the AREDS trial.

Dr. Dowling: Right.

Mr. McManus: It was supported by industry yet they could only come to the Data Monitoring Committee meetings and look at the data. They couldn't see the data ahead of time or anything. What if that combination of vitamins killed people or didn't _____.

Dr. Dowling: The vitamin A, vitamin E RP trial is a good example, where vitamin E seems to be negative for certain people, whereas vitamin A might be positive for some people. I think the point I'm making is that if we are to move forward on translational research it has to be with partnerships between the private sector, the university and the government.

Mr. McManus: And I was just saying that maybe the law needs to be changed to facilitate that.

Dr. Dowling: Perhaps, yes, to make it easier. I'll say something else that has been bothering me recently. This is all the regulations that now have been put in with regard to NIH grants, with what Intramural people can do in terms of consulting and so on and so forth, I often get the feeling that Congress treats NIH like a welfare program. I'm signing so many disclosure forms now when I send in a grant. It's as though I'm going to cheat on the research I do, that I'm going to torture my animals, that I'm going to be doing company-based research in my lab or what have you. I mean, that whole atmosphere is discouraging - we're in this to try to move the scientific enterprise forward and yet, why all these rules and regulations? Congress has been very generous, there's no question about that, but why so much distrust?

Mr. McManus: It may be—it is germane to this discussion or this discussion is germane to this book. Because I said, we're going to spend all this time writing this book and it may be that what the vehicle or the support of research in 20 years from now is completely different with all these other things, like the cumbersome regulations, the need to have the drug companies hands off on the clinical trials but to have the clinical trials done. The state money coming out, the old Nixon, send all the money out of Washington right to the states anyhow and if you did that then you wouldn't have all these regs. So all of these things might kind of come together and people out to be thinking about what that might look like.

Dr. Dowling: The amount of red tape that we now have is way beyond what it should be. I was talking with a former graduate student of mine who was in the Department of the Treasury and has been involved in start-up companies. We were talking about starting up a biotech company. He asked how easily and quickly could one get some money from the Eye Institute to do a pilot project. I said "Well, you've got to think that it's at least a year away". You first must write a proposal, then have it reviewed and finally funded after Council approval. He said it was very different in the Treasury Department where he was involved in a start-up company to provide software that would be very potentially useful for something the Treasury Department needed to do. He said they could write us a contract for a million dollars just by an executive decision.

Mr. McManus: I used to do that. I did that for about two or three minutes, not for a million but for several hundred thousand.

Dr. Dowling: You couldn't do that today in the Eye Institute.

Mr. McManus: I would have to go to the Council to get approval.

Dr. Dowling: Could you do that today? I didn't even realize that you could do that.

Mr. McManus: Yeah. You have to get a concept clearance. And we did that—you might not have been there and you might not have, but we did that. We were the only institution supporting the World Health Organization and we wanted to support them on doing kind of small power studies around the world on feasibility.

Dr. Dowling: Yes, I do remember that.

Mr. McManus: So we did a contract with them for…

(SIDE A ENDS HERE/THERE IS NO FURTHER DICTATION ON SIDE B)

Interview ends.